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(54) Title: <b>CATALYTIC RING OPENING POLYMERIZATION OF LACTONES, CARBONATES, ETHERS, MORPHOLINE-2,5-DIONES AND ANHYDRIDES AND CATALYST THEREFOR</b> (57) Abstract <p>The invention relates to a method for the catalytic ring opening polymerization of lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides comprising contacting these compounds under polymerizing conditions with at least one metal coordinating compound initiator and at least one co-initiator, wherein the co-initiator replaces at least one ligand of the metal coordinating compound by a replacement ligand, which is less sterically hindering, in order to form a catalytic unit, so that the active part of the catalytic unit formed in this way is capable of approaching easier the compound undergoing catalytic ring opening.</p>		

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CATALYTIC RING OPENING POLYMERIZATION OF LACTONES,  
CARBONATES, ETHERS, MORPHOLINE-2,5-DIONES AND ANHYDRIDES  
AND CATALYST THEREFOR

The present invention relates to a method for the catalytic ring opening polymerization of lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides, to a catalyst therefor, to a method for preparing the  
5 catalyst and to products resulting from the catalytic ring opening polymerization.

Lactide and  $\epsilon$ -caprolactone polymerization using homogenous yttrium and lanthanide alkoxides as catalysts is known (McLain, S.J.; Drysdale, N.E. Pol. Prep. 1992,  
10 33, 174; McLain, S.J.; Drysdale, N.E. Pol. Prep. 1992, 33, 463; and Yasuda, H.; Firo, M.; Yamamoto, H.; Nakamura, A.; Miyake, S.; Kibino, N. Macromolecules 1992, 25, 5115).

The catalytic polymerization of L-lactide by  
15 yttrium isopropoxide, a cluster compound wherein five yttrium atoms are joined to a single central oxygen atom,  $Y_5(\mu-O)(O^iPr)_{13}$  has been studied by Stevels W.M.; Ankoné, M.J.K.; Dijkstra, P.J.; Feijen, J. Macromol. Chem. Phys. 196, 1153 (1995). This catalytic polymerization appears  
20 to be a living process wherein each isopropoxide ligand initiates polymerization and each polymer chain comprises an isopropoxy carbonyl end group.

The use of 2,6-di-*t*-butylphenoxo yttrium ( $Y(OAr)_3$ ) as a catalyst in the ring opening polymerization  
25 of L-lactide has been evaluated by Stevels et al. Study has been carried out into the use of this compound as a catalyst, since it was known that it is not associated in solution and since its molecular structure is known (Hitchcock, P.B.; Lappert, M.F.; Smith, R.G. Inorg. Chim.  
30 Acta, 1987, 139, 183), these being qualities which make it catalytically interesting. Tris(2,6-di-*t*-butylphenoxo)yttrium can be purified by in vacuo

sublimation at 250°C and is accordingly thermally very stable. It has been shown that no direct reaction can occur between the 2,6-di-t-butylphenoxo ligands and one of the carbonyl carbon atoms of L-lactide, probably due to steric hindrance. It has not been ruled out that in this instance, polymerization is initiated by trace pollutants. In this manner it is not possible to control the molecular weight and the identity of the end groups of the polymers obtained (Stevens , Ankoné, Dijkstra and Feijen).

Further research into the activity of the catalyst has shown that its working can be further improved when the sterically hindering ligands around the central metal atom are replaced by a less sterically hindering group which makes better accessibility to the receiving part of the compound, subjected to the ring opening, possible by the catalyst.

The present invention therefore relates to a method for the catalytic ring opening polymerization of lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides comprising contacting these compounds under polymerizing conditions with at least one metal coordinating compound initiator and at least one co-initiator, wherein the co-initiator replaces at least one ligand of the metal coordinating compound by a replacement ligand, which is less sterically hindering, in order to form a catalytic unit, so that the active part of the catalytic unit formed in this way is capable of approaching easier the compound undergoing catalytic ring opening.

The advantages of the present method are that:

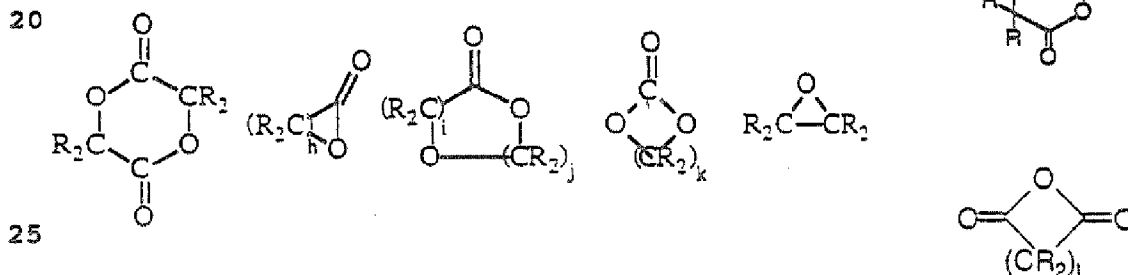
- a large variety of polymers can be made without necessitating the preparation of a number of different catalysts;

- the molecular weight and the end group identity are determined by the amount and chemical structure of the co-initiators;

- an improved catalytic activity is provided;

- the number of active sites per metalcenter in the catalyst is substantially under control, whereby structurally well defined polymers, specifically so called block co-polymers, can be obtained; and
- 5 - for each specific endgroup of a determined polymer, no new catalyst is needed to be prepared and isolated whereby problems during the synthesis of these types of compounds, which are often difficult to purify and to characterize, are obviated. Such problems can lead
- 10 to the situation that the behavior of the catalyst, especially its activity and the number of active sites per metalcenter, are difficult to predict and as such, the characteristics of the resulting polymer molecules (molecular weight, molecular weight ratio and end group
- 15 identity) are also difficult to predict.

Preferably, the lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides are selected from the group consisting of compounds with the general formulas:



wherein h is 2, 4 or 5, i is 1 or 2, j is 1 or 2, k is 2, 3 or 4, and l is 2, 3 or 4 and each R is an H or hydrocarbyl or substituted hydrocarbyl or hydrocarbyl

30 with protected functionality with a maximum of 30 carbon atoms.

Preferred lactones are those wherein R is hydrogen or methyl, and lactones wherein  $\epsilon$ -caprolactone,  $\delta$ -valerolactone, glycolide, and lactides, such as L-

35 lactide, D-lactide, meso-lactide and rac-lactide are especially preferred.

Preferred carbonates are those wherein R is hydrogen or methyl and especially preferred are tri-

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methylene carbonate, ethylene carbonate, propylene carbonate, tetramethylene carbonate and 2,2-di-methyl tri-methylene carbonate.

The metal coordinating compound initiator preferably has the general formula  $MZ_3$ , wherein M is preferably selected from the group consisting of scandium, yttrium and the lanthanide series (atomic numbers 57-71) of rare earth metals, and wherein Z are preferably the same or different sterically demanding or bidentate or polydentate ligands.

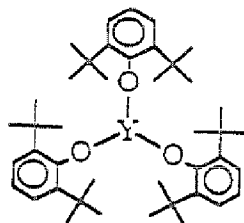
It will be obvious to the person skilled in the art that when more than one type of Z-group is present, re-arrangement reactions can take place. Under re-arrangement reactions is understood that an exchange of Z-groups can take place between the metal atoms, so that it is in theory possible to obtain every combination of Z-groups at every random metal atom. It will also be clear to the person skilled in the art that one or more ligands can non-covalently coordinate to the metal center, such as solvents, monomers, protonated ligands or co-initiators, without affecting the formulation of the initiator as  $MZ_3$ .

The metals in the coordination compound are most preferably the initiators yttrium and lanthanum.

The ligands Z are preferably selected from the group consisting aryl alkoxides, alkyl alkoxides, amides, hydrocarbons, betadiketonates, benzamindinate, cyclopentadienide and substituted cyclopentadienides, porphyrines and trispyrazolylborates.

Preferred ligands are sterically hindering 2,6-di-substituted phenoxide ions, whereby possible other substitutions than by hydrogen at the 3, 4 and 5 sites are not excluded. Most preferably, the initiator has three sterically hindering 2,6-di-substituted phenoxide ions coupled to the yttrium atom, for example yttrium tris 2,6-di-tert-butyl phenoxide.

5



The co-initiator is preferably a proton donor  
 10 and is preferably selected from the group consisting of  
 compounds having the general formula  $(H_xX)_yR'$ , and water,  
 wherein

- x and z are 1 when X is an oxygen or sulfur atom,
- 15 - x and z are 1 or 2 when X is a nitrogen atom,
- y is 1,2,3,4 or more, and
- R' is selected from the group consisting of hydrogen, hydrocarbyl with a maximum of 50 carbon atoms and substituted hydrocarbyl with a maximum of 50 carbon  
 20 atoms.

Preferred co-initiators are mono-, di- or polyfunctional alcohols including biologically active alcohols such as hormones, vitamins or anti-inflammatory compounds.

25 Preferred are polymers with a reactive chain end such as some polyesters, polyethers and polyamides or combinations of these for the synthesis of block copolymers. Most preferably the co-initiators are hydroxyl terminated polyethylene glycols, poly-ε-  
 30 caprolactones or poly-lactides.

It will be clear to the person skilled in the art that the initiators preferably work as proton receivers from the co-initiators and that it is preferred that such a proton is rapidly transferred. The protonated  
 35 ligand which results from this proton transfer, preferably has no effect on the polymerization process and it can be preferably easily removed from the reaction mixture.

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The method according to the present invention can either be carried out as a solution polymerization or melt polymerization wherein the solution polymerization is preferably carried out at a temperature of between  
5 -80°C and 180°C and wherein the melt polymerization is carried out at a temperature of between 50°C and 200°C.

The initiator is preferably at least partially soluble in the solvent used with solution polymerization, or in the melt monomer mixture.

10 Preferred solvents for use in the present invention are solvents wherein the monomer which undergoes catalytic ring opening polymerization, the resulting polymer, the initiator and the co-initiator are soluble. Preferred solvents are chlorinated hydrocarbons,  
15 aliphatic ethers, aromatic solvents and some hetero atom comprising solvents.

It is preferred that the reaction is carried out in the presence of a dry inert gas such as nitrogen or argon which protects the reaction. Moisture is  
20 detrimental for the activity of the catalyst due to hydration, and can limit the molecular weight of the polymer produced.

The start materials are preferably dry. Drying methods are known to the person skilled in the art and  
25 comprise distillation with suitable drying means, crystallization and sublimation.

The invention further relates to a method for preparing catalytic units by contacting a metal coordinating compound initiator and co-initiator such as  
30 above described, to the catalytic unit resulting from this method, and to the polymers produced.

The invention will now be illustrated with respect to practical examples of catalytic ring opening polymerization.

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## EXAMPLES

### INTRODUCTION

Ring opening polymerization of L-lactide (L-La) was initiated by a combination of tris(2,6-di-t-butylphenoxo)yttrium ( $Y(OAr)_3$ ) (1) and n-butanol, i-propanol, t-butanol, ethylene glycol, polyethylene glycol, N,N-dimethyl amino ethanol and methoxy ethanol respectively. The polymerizations were carried out in dichloromethane solution at 22°C and conversion was 92-100% within 5 minutes. The endgroups of the resulting polymers consisted only of the alkyl ester group of the added alcohol and lactyl OH groups. Polymerization was preceded by a rapid alcohol exchange and in situ formation of yttrium alkoxides from the added alcohol and 2,6-di-t-butylphenol ( $HOAr$ ). The presence of 2,6-di-t-butylphenol in the reaction mixture did not influence the polymerization characteristics. The ring opening polymerization of  $\epsilon$ -caprolactone ( $\epsilon$ -CL),  $\delta$ -valerolactone ( $\delta$ -VL) and trimethylene carbonate (TMC) proceeded in a corresponding manner. Block copolymers of poly( $\epsilon$ -caprolactone) and poly(L-lactide) were prepared by sequential polymerization of the monomers. Melt polymerization of L-lactide was carried out at 130°C and 180°C using 1-decanol as initiator. The conversion was complete within 5 minutes and once again the end group of the resulting polymers consisted only of the alkyl ester group from the added alcohol and lactyl OH groups. Random copolymers of L-lactide, D-lactide (D-LA) and glycolide (GLY) were also prepared in the melt.

### MATERIALS AND METHOD

The reagents L-lactide and D-lactide (Purac Biochem b.v., the Netherlands) and glycolide (Boehringer Ingelheim, Germany) were used as received from the supplier.  $\epsilon$ -Caprolactone and  $\delta$ -valerolactone (Merck-Schuchardt, Darmstadt, Germany) were dried over calciumhydride and distilled before use. Trimethylene carbonate was prepared as described earlier and purified

by crystallization in diethyl ether. Yttrium isopropoxide (Aldrich, Brussels, Belgium) was washed with toluene and filtered in order to remove insoluble material and was dried in vacuo for 48 h at 35°C. Tris(2,6-di-t-butylphenoxo)yttrium was prepared as described earlier. Toluene, dioxane and diethyl ether were distilled preceeding the use of sodium benzophenonketyl and calciumhydride dichloromethane.

Poly(ethylene glycol) ( $M_n = 1000$ ) (Janssen Chimica, 's-Hertogenbosch, the Netherlands) was twice stripped with toluene and dried for 18 hours in the melt at 65°C in vacuo (0,5 mm Hg). 2-propanol and 1-butanol were dried over  $MgSO_4$  and distilled. 1,1-di-methyl-ethanol (t-butanol) was distilled from its sodium salt. Ethylene glycol was dried over molecular sieves (30nm) and distilled under reduced pressure. 2,6-di-t-butylphenol (Merck-Schuchardt, Darmstadt, Germany) was used as received. All experiments were carried out in an inert oxygen or argon atmosphere. Polymerizations were carried out in a Braun 150 GI glove cabinet.

#### Solution polymerizations

In a typical experiment, an amount of alcohol was added to a solution of 20 mmol lactone in 20 ml dichloromethane which corresponded to a mole ratio between the monomer and the initiator ( $[M]/[I]$ ) of 50. To this mixture was added 2.7 ml of a 0,05 M tris(2,6-di-t-butylphenoxo)yttrium solution in toluene, corresponding to a mole ratio between monomer and catalyst ( $[M]/[C]$ ) of 150. The polymerization began immediately and after 2 to 5 minutes the polymerization was stopped by addition of an equal volume of a 0,1 N HCl solution. The organic phase was precipitated in a 10 times excess of cold methanol and the product was dried at 40°C in vacuo.

#### Melt polymerizations

In a typical experiment the monomer(s) and 1-decanol were preweighed in a reaction vessel with a round

bottom provided with an inlet for an inert gas and a rubber septum. The reaction mixture was heated in an oil bath under an Ar outstream and a suitable amount of a 0.14 M solution of  $Y(OAr'')_3$  in toluene was added. The reaction mixture became almost immediately viscous and the reaction was carried out for a little time (5 minutes at 180°C, 10 minutes at 130°C). The reaction was stopped by rapid cooling to 0°C. The resulting polymer was dissolved in 50 ml of a solution of acetic acid in chloroform (2% vv) and washed with a 0.1 N HCL solution and precipitated in 10 times excess cold methanol and the product was dried at 40°C in vacuo.

#### Characterization

The average polymerization degree was determined by  $^1H$ -NMR endgroup analysis.  $^1H$ -NMR spectra were recorded on a Bruker AC 250 which worked at 250 MHz ( $^1H$ ) or 62,5 MHz ( $^{13}C$ ). Gelpermeation-chromatography (GPC) was used in order to determine the molecular weights and molecular weight divisions ( $M_w/M_n$ ). GPC measurements were carried out with THF as the eluent (2.0) ml/min with a Waters 510 pump, an HP 1050 autosampler, four Waters  $\mu$ Styragel columns ( $10^5$ ,  $10^4$ ,  $10^3$  and  $5 \times 10^2$ ) in series, a Waters 410 differential refractometer, and a Viscotek Viscometer Detector H502. The columns were calibrated with poly(styrene) standards by means of universal calibration technique. The samples of pure poly(L-lactide)s required gentle warming before they dissolved.

#### EXAMPLES

Example 1: Synthesis of a poly(L-lactide) in solution.

To a stirred solution of 2,49 g (20 mmol) L-lactide in 20 ml dichloromethane was added 1 ml of a 0.4 M solution of n-butanol (0.4 mmol) in toluene. To this mixture was added 2.7 ml of a 0.05 M solution of yttrium tris (2,6-di-tertbutylphenoxo) (0.135 mmol) in toluene. After 5 minutes the polymerization was stopped by

addition of 0.5 ml water and vigorous stirring. After taking a sample for NMR determination of the conversion, the polymer solution was washed with a 0.1 N HCl solution in water, followed by precipitation in a ten times excess of cold methanol and a night's drying in a vacuum oven at 40°C. Conversion: > 99%, isolated yield 2,62 g (90%) white polymer, calculated mole weight 7200 g/mol, mole weight found: 6600 (NMR), 8600 (GPC) and a polydispersity of 1.16.

10

Example 2: Synthesis of poly-L-lactide in solution.

To a stirred solution of 2.94 g (20 mmol) L-lactide in 40 ml dichloromethane was added 8.1 ml of a 0.05 M solution of i-propanol in toluene. To this mixture was added 2.7 ml of a 0.05 M solution of lanthanum tris(2,6-di-terbutylfenoxo) (0.135 mmol) in toluene. After 5 minutes the polymerization was stopped by addition of 0.5 ml water and vigorous stirring. After taking a sample for NMR determination of the conversion, the polymer solution was washed with a 0,1 N HCl solution in water, followed by precipitation in a ten times excess cold methanol and a night's drying in a vacuum oven at 40°C. Conversion: > 99%, isolated yield 2.75 g (95%) white polymer, calculated mole weight 5200 g/mol, mole weight found: 7100 (NMR), 10800 (GPC) and a polydispersity of 1,14.

Example 3: Synthesis of poly( $\epsilon$ -caprolacton) in solution.

To a stirred solution of 2.28 g (20 mmol)  $\epsilon$ -caprolacton in 20 ml dichloromethane was added 8.1 ml of a 0.05 M solution of isopropanol (0.40 mmol) in toluene. To this mixture was added 2.7 ml of a 0.05 M solution of yttrium tris(2,6-di-tertbutylfenoxo) (0.135 mmol) in toluene. After 5 minutes the polymerization was stopped by addition of 0.5 ml water and vigorous stirring. After taking of a sample for the NMR determination of the conversion, the polymer solution was washed with 0.1 N HCl solution in water, followed by precipitation in a ten

times excess of cold hexane and a night drying in a vacuum oven at 40°C. Conversion: >99%, isolated yield 1.41 g (62%) white polymer, calculated mole weight 5700 g/mol, mole weight found: 6000 (NMR), 7400 (GPC) and a polydispersity of 1.14.

Example 4: Synthesis of an AB poly( $\epsilon$ -caprolacton-*b*-L-lactide) diblock copolymer in solution.

To a stirred solution of 2.28 g (20 mmol)  $\epsilon$ -caprolacton in 20 ml dichloromethane was added 8,1 ml of a 0.05 M solution of isopropanol (0.40 mmol) in toluene. To this mixture was added 2,7 ml of an 0.05 M solution of yttrium tris(2,6-di-tertbutylfenoxo) (0,135 mmol) in toluene. After 3 minutes a sample was taken for NMR analysis and a solution of 2.94 g (20 mmol) L-lactide in dichloromethane was added to the reaction mixture. After a further 5 minutes stirring, the polymerization was stopped by addition of 0.5 ml water and vigorous stirring. After taking a sample for NMR determination of the conversion, the polymer solution was washed with 0.1 N HCl solution in water, followed by precipitation in a ten times excess of cold methanol and a night drying in a vacuum oven at 40°C. Conversion: 100 and 99% respectively, isolated yield 4.74 g (94%) white polymer, calculated mole weight 12900 g/mol, mole weight found: 13900 (NMR, 17600 (GPC) and a polydispersity of 1.16.

Example 5: Synthesis van poly(L-lactide) with less initiator with respect to the catalyst in solution.

To a stirred solution of 2.94 g (20 mmol) L-lactide in 20 ml dioxane, was added 3 ml of a 0.05 M solution isopropanol (0.15 mmol) in toluene. To this mixture was added 2.7 ml of a 0.05 M solution of yttrium tris (2,6-di-tertbutylfenoxo) (0.135 mmol) in toluene. After 8 minutes the polymerization was stopped by addition of 0.5 ml water en vigorous stirring. After taking a sample for NMR determination of the conversion, the polymer solution was washed with 0.1 N HCl solution

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in water, followed by precipitation in a ten times excess of cold methanol and a night drying in a vacuum oven at 40°C. Conversion: 99%, isolated yield 1.84 g (85%) white polymer, calculated mole weight 19200 g/mol, mole weight found: 24000 (NMR), 21000 (GPC) and a polydispersity of 1.37.

Example 6: Synthesis of poly(L-lactide) in the melt at 180°C.

- 10 To a melted mixture of 4.38 g (30.4 mmol) of L-lactide and 95 mg (0.59 mmol) 1-decanol at 180°C was added 1.36 ml of a 0.15 M solution of yttrium tris (2,6-di-tertbutylphenoxo) (0.20 mmol) in toluene. After 5 minutes the reaction was stopped by rapid cooling to 0°C.
- 15 The reaction mixture was dissolved in 40 ml 2% v/v solution of acetic acid in chloroform, and washed with a 0.1 N HCl solution in water, followed by precipitation in an ten times excess of cold methanol and a night drying in a vacuum oven at 40°C. Conversion: 97%, isolated yield
- 20 3.81 g (87%) white polymer.

### Results and discussion

- It is known that with L-lactide polymerizations with anionic catalysts, racemization can occur by
- 25 withdrawing the proton joined to the chiral carbon atom instead of nucleophilic attack on the carbonyl carbon atom, which is the propagation step in the polymerization process so as shown in Fig. 1. Yttrium compounds which comprise yttrium-hydrogen, yttrium-carbon and yttrium-
- 30 nitrogen compounds are very reactive with respect to substrates which contain activated hydrogen atoms. In a study into  $\epsilon$ -caprolactone polymerization by divalent samarium complexes, polymers were obtained with a broad molecular weight distribution without specific end
- 35 groups. This points to  $\alpha$ -H withdrawal. Hence, according to the present invention, yttrium compounds with strong basic qualities are avoided. Due to their large ion radius and Lewis acidity, yttrium and lanthanide

compounds have the tendency to strongly associate in solution. This can be disadvantageous for the catalyst activity. The use of tris(2,6-di-t-butylphenoxo)yttrium ( $Y(OAr)_3$ ) as catalyst in the ring opening polymerization of L-lactide has also been studied since it is known that it is not associated in solution. Moreover, its molecular structure has been determined by single crystal X-ray diffraction.

$Y(OAr)_3$  is somewhat active in L-lactide polymerization. The reaction is complete in 10 hours in dichloromethane and no specific endgroups were detected by means of  $^1H$ -NMR spectroscopy, but racemization is also present. A much higher molecular weight was found by gel permeation chromatography than expected from the initiator concentration when the phenoxide ligand initiates the polymerization ( $M_{n,calc} = 7600$ ,  $M_{n,found} = 29,300$ ). In this instance it appears probable that the polymerization is initiated by protic impurities. The results indicate that a reaction between the nucleophilic carbonyl carbon atom and the oxygen atom in the phenoxide ligand is not possible. In an independent experiment, it appeared that 2,6-di-t-butyl-phenol had no influence on the polymerization of L-lactide by yttrium isopropoxide (Fig.2) when reaction rate, molecular weight, molecular weight distribution or polymer endgroup identity were taken into account. This can be ascribed to the steric hindrance around the hydroxyl group in 2,6-di-t-butyl-phenol. The lack of reactivity of the yttrium-oxygen bond in  $Y(OAr)_3$  together with the fact that alcohol-alkoxide ligand exchange in soluble metal alkoxides is, in general, very rapid, initiated another approach. In situ formation of a small alkoxide ligand by alcohol/alkoxide exchange can be used to initiate the polymerization after removal of the sterically hindered 2,6-di-t-butyl-phenol from the metal center. Even when an equilibrium exists between the polymer chain end and the 2,6-di-t-butyl-phenol, this would not necessarily slow down the polymerization when the exchange reaction is quick and reversible.

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Well defined polymers can be prepared by adding  $Y(OAr)_3$  to a mixture of alcohol and 50 equivalents L-lactide. Polymerization began immediately and transformation was complete within 2 to 5 minutes. The results of the polymerization reactions are shown in Tab.1. Initiation can occur with a wide variety of compounds comprising primary, secondary or tertiary hydroxyl groups, as is shown by n-butanol, i-propanol, t-butanol, ethylene glycol and poly(ethylene glycol) in table 1. In general, low molecular weights which were determined with the aid of NMR spectroscopy, were close to the values which were calculated on the basis of the alcohol concentration apart from t-butanol and ethylene glycol where large deviations between the calculated values and the values found occurred. This was ascribed to the inefficient initiation due to steric hindrance in the case of t-butanol and to the low solubility of the initiator in dichloromethane in the case of ethylene glycol. The polymers had unimodal, symmetrical molecular weight distributions with a polydispersity between 1.14 and 1.37. Although there was a discrepancy between the molecular weights, which were determined by NMR and GPC, the values determined by these methods, were in general similar. The presence of 2,6-di-t-butyl-phenol did not influence the polymerizations and was easily removed by precipitation from the polymer. The endgroups of the resulting polymers consisted only of the alkyl ester group of the added alcohol and lactyl hydroxyl groups. Based on these observations, a general reaction scheme was proposed such as shown in Fig. 3. Substoichiometric amounts of alcohol with respect to the phenoxide ligands can be used in order to initiate the polymerization. When, for example, instead of three equivalents of isopropanol, one equivalent per Y is used, the molecular weight of the resulting polymer triples. The activity of the described catalyst system is not exceeded in coordination polymerization of L-lactide. Initiators such as  $Y(OCH_2CH_2NMe_2)_3$  comprise a coordinating group which

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compete with monomers for coordination sites and in this manner possibly slow down the polymerization. In an independent experiment, the addition of  $\text{NEt}_3$  slowed down the polymerization of L-lactide by yttrium isopropoxide by at least a factor of two.

The polymerization of other monomers such as  $\epsilon$ -caprolactone,  $\delta$ -valerolactone and trimethylene carbonate is easily achieved as well. Complete conversion of  $\epsilon$ -caprolactone is achieved within five minutes. Diblock copolymers of poly( $\epsilon$ -caprolactone) and poly(L-lactide) can be prepared by addition of L-lactide to a just polymerized poly( $\epsilon$ -caprolactone) solution, which indicates that the polymerization has living characteristics, which was also shown for other yttrium alkoxide initiators. When an attempt was undertaken to polymerize  $\epsilon$ -caprolactone and L-lactide together, only poly(L-lactide)s were formed and the catalyst activity was significantly reduced. Caprolactone can not be polymerized by  $\text{Y}(\text{OAr})_3$  in the presence of a poly(L-lactide) with a hydroxyl end. This corresponds to earlier observations. The activity of the catalyst system in  $\delta$ -valerolactone polymerizations was lower than for L-lactide or  $\epsilon$ -caprolactone, but it is one of the very few examples of  $\delta$ -valerolactone homopolymerization by coordination type catalysts. A number of results were obtained in studies with anionic and cationic catalysts. It is said of this that it is a substantially strain free monomer which would explain the reduced activity of the catalyst system for this monomer. Deviating coordination behavior of this monomer, by steric and electronic effects, could also result in a deviating reactivity pattern.

Melt polymerization of L-lactide and copolymerizations with glycolide and D-lactide were carried out at 130°C and 180°C with  $\text{Y}(\text{OAr})_3$  and 1-decanol as the catalyst system. The results of the polymerization reactions are given in table 2. The conversion was almost complete in all experiments. As earlier, the presence of

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2,6-di-t-butyl-phenol had no influence on the experiments and was easily removed by precipitation from the polymer. The end groups of the resulting polymers consisted only of the alkyl ester group of the added alcohol and lactyl hydroxyl groups. No 1-decanol which had not reacted, could be detected with the aid of  $^1\text{H-NMR}$  spectroscopy. The proposed reaction mechanism for solution polymerization also appears therefore to be applicable for melt polymerization. Copolymers of L-lactide and glycolide were also prepared by melt polymerization. Glycolide conversion was complete whilst a small amount of L-lactide remained unreacted. The greater reactivity of glycolide in copolymerizations with lactide was earlier observed.

15

### Conclusions

The combination of  $\text{Y}(\text{OAr})_3$  and alcohols is a flexible and very efficient catalyst system for the ring opening polymerization of L-lactide and other lactones and carbonates with a good control over the molecular weights and the end group identities. The generality of this method was shown for a number of experiments with differing alcohols, solvents, monomers and reaction temperatures. It is proposed that the polymerization is preceded by a rapid alcohol exchange and in situ formation of the yttrium alkoxides of the added alcohol and 2,6-di-t-butylphenol ( $\text{HOAr}$ ). The presence of 2,6-di-t-butylphenol in the reaction mixture did not influence the polymerization characteristics.

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Table 1. Results of the polymerizations with 1 as catalyst

Monomer	Co-initiator	Reaction time (min)	Monomer conversion (%)	$M_n^{\text{calculated}}$ ( $\text{g/mol}$ ) $\times 10^{-3}$	$M_n^{\text{GPC}}$ ( $\text{g/mol}$ ) $\times 10^{-3}$	$M_w/M_n$
L-LA	n-BuOH	5	100	7.2	6.6	1.16
	i-PrOH	2	100	7.2	8.4	1.24
	i-PrOH	8	99	19.2	21.0	1.37 <sup>3)</sup>
	t-BuOH	5	99	7.2	13.0 <sup>1)</sup>	1.21
	HOEtOH	5	92	14.4	25.2 <sup>2)</sup>	1.28
	PEG1000	2	94	15.4	18.5	1.16
	Me <sub>2</sub> NEtOH	3	99	6.5	8.4	1.04
	MeOEtOH	3	99	6.5	7.9	1.11
$\epsilon$ -CL	i-PrOH	5	100	5.7	6.0	1.14
$\delta$ -VL	i-PrOH	5	71	3.5	n.d.	1.10
	i-PrOH	20	81	8.1	10.3	
TMC	i-PrOH	5	86		11.5	
$\epsilon$ -CL/L-LA	i-PrOH <sup>4)</sup>	3/5	100/99	12.9	13.9	1.16
$\epsilon$ -CL/L-LA	i-PrOH <sup>5)</sup>	5	0/50		n.d.	
$\epsilon$ -CL	PLLA	48 hour	0		n.d.	

1) the large deviation between calculated and found values is ascribed to the steric hindering of the catalytic unit

2) the large deviation between calculated and found values is ascribed to the weak solubility of the initiator in dichloromethane

3) the reaction mixture was only de-activated after 16 hours.

4) monomers sequentially added

5) monomers simultaneously added

Table 2. Results of the melt polymerizations with 1 as catalyst. 1-Decanol was used as co-initiator in all cases.

Monomer <sup>1)</sup>	Temperature	Reaction time (min)	Monomer conversion (%)
L-LA	180	5	97
	130	10	98
L-LA <sup>90</sup> /GLY <sup>10</sup>	180	5	96/100
L-LA <sup>50</sup> /GLY <sup>50 2)</sup>	130	10	n.d.
L-LA/D-LA	100	30	80

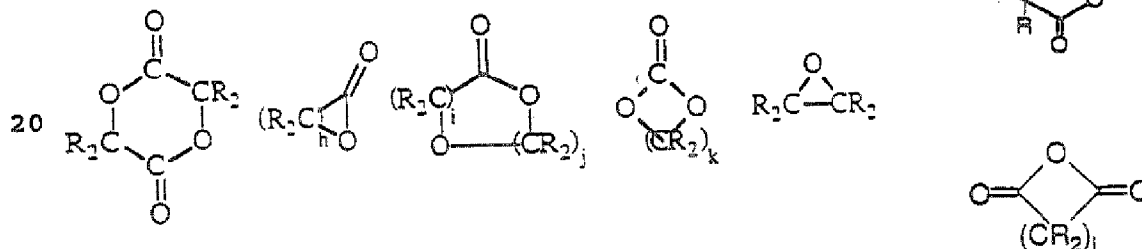
1) the numbers in superscript following the abbreviations of the differing monomers, show the composition of the start mixture in mole percentages.

2) due to the very weak solubility of this polymer it was only characterized with differential calory metry. A glass transition temperature of 50°C was established.

## CLAIMS

1. Method for the catalytic ring opening polymerization of lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides comprising contacting these compounds under polymerizing conditions  
 5 with at least one metal coordinating compound initiator and at least one co-initiator, wherein the co-initiator replaces at least one ligand of the metal coordinating compound by a replacement ligand, which is less sterically hindering, in order to form a catalytic unit,  
 10 so that the active part of the catalytic unit formed in this way is capable of approaching easier the compound undergoing catalytic ring opening.

2. Method according to claim 1, wherein the lactones, carbonates, ethers, morpholine-2,5-diones and  
 15 anhydrides are selected from the group consisting of compounds with the general formulas:



wherein h is 2, 4 or 5, i is 1 or 2, j is 1 or 2, k is 2,  
 25 3 or 4, and l is 2, 3 or 4 and each R is an H or hydrocarbyl or substituted hydrocarbyl or hydrocarbyl with protected functionality with a maximum of 30 carbon atoms.

3. Method according to claim 1 or 2, wherein  
 30 the metal coordinating compound has the formula  $\text{MZ}_3$ , wherein

- M is preferably selected from the group consisting of scandium, yttrium and the lanthanide series (atomic number 57-71) of rare earth metals, and

- Z are preferably the same or different sterically demanding or bidentate or polydentate ligands.

4. Method according to claim 3 wherein the ligands Z, are selected from the group consisting of aryl alkoxides, alkyl alkoxides, amides, hydrocarbons, betadiketonates, benzamidinates, cyclopentadienide and substituted cyclopentadienides, porphyrines and trispyrazolylborates.

5. Method according to claim 1-4 wherein the co-initiator is a proton.

6. Method according to claim 5 wherein the proton donor is selected from the group consisting of compounds having the general formula  $(H_xX)_yR'_z$  and water, wherein

- x and z are 1 when X is an oxygen or sulfur atom,
- x and z are 1 or 2 when X is a nitrogen atom,
- y is 1,2,3,4 or more, and
- R' is selected from the group consisting of hydrogen, hydrocarbyl with a maximum of 50 carbon atoms and substituted hydrocarbyl with a maximum of 50 carbon atoms.

7. Method according to claims 1-6 wherein the lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides are monomers.

8. Method according to claims 1-6 wherein the lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides are co-monomers.

9. Method according to claim 8 wherein the lactones are selected from the group consisting of  $\epsilon$ -caprolactone,  $\delta$ -valerolactone, glycolide and lactides.

10. Method according to claims 2-9 wherein the R in the lactones is hydrogen.

11. Method according to claim 10 wherein the lactides are L-lactide, D-lactide, meso-lactide, and rac-lactide.

12. Method according to the claims 2-11 wherein the R in the carbonates is hydrogen or methyl.

13. Method according to the claims 2-12, wherein the carbonates are selected from the group consisting of trimethylene carbonate, ethylene carbonate, propylene carbonate and 2,2 dimethyltrimethylene carbonate.

14. Method according to the claims 1-13 carried out in the presence of a solvent.

15. Method according to claim 14 wherein the polymerization temperature is between - 80°C and 180°C.

16. Method according to claims 1-13 carried out as a melt polymerization.

17. Method according to claim 16 wherein the polymerization temperature is between 50°C and 200°C.

18. Method according to claim 15 wherein the preferred solvent are chlorinated hydrocarbons, aliphatic ethers, aromatic solvents and some hetero-atom comprising solvents.

19. Method according to one of the claims 1-15 wherein the metal coordinating compounds are monomers in solution or in equilibrium with the monomer species.

20. Method according to claim 14 wherein monomers, polymers, initiator and co-initiator are dissolvable in the solvent.

21. Method for producing a catalytic unit by contacting at least one metal coordinating compound with the general formula  $MZ_n$ , wherein:

- M is selected from the group consisting of scandium, yttrium and the lanthanide series of rare earth metals (atomic numbers 57 to 71) and

- Z are similar or differing sterically demanding or bidentate or polydentate ligands with at least one proton donor.

22. Method according to claim 1 wherein the ligand Z is selected from the group consisting of 2,6 substituted aryl alkoxides, alkyl alkoxides, amides, hydrocarbons, betadiketonates, benzamidinate, cyclopentadienide and substituted cyclopentadienides, porphyrines and trispyrazolylborates.

23. Method according to claim 21 or 22, wherein the proton donor is selected from the group consisting of compounds with the general formula  $(H_X X)_Y R'$ , and water, wherein

- 5                   - x and z are 1 if X is an oxygen or sulfur atom,  
                  - x and z are 1 or 2 if X is a nitrogen atom,  
                  - y is 1,2,3,4 or more, and  
                  - R' is selected from the group consisting of  
10 hydrogen, hydrocarbyl with a maximum of 50 carbon atoms and substituted hydrocarbyl with a maximum of 50 carbon atoms.

24. A catalytic unit with the general formula  $MZ_m (XR)_n$  obtainable by the method according to claims 21-  
15 23, wherein Z originates from the metal coordinating  $MZ_3$  according to claim 21 and X originates from the proton donor according to claim 23, and wherein  $m + n = 3$ .

25. The use of a catalytic unit according to claims 21-24 in a method for the catalytic ring opening  
20 polymerization of lactones, carbonates, ethers, morpholine-2,5-diones and anhydrides according to the claims 1-20.

26. Method for producing block copolymers by the subsequent introduction of two or more lactone,  
25 carbonate, ether, morpholine-2,5-diones and anhydride monomers in the polymerization method according to the claims 1-20.

27. Method for preparing random co-polymers by the simultaneous introduction of two or more lactones,  
30 carbonate, ether and anhydride monomers in the polymerization method according to the claims 1-20.

28. Polymers, block copolymers and random co-polymers obtainable by the method according to the claims 1-20, 26 and 27.

35                   29. Polymers according to claim 28 obtainable by the method according to the claims 1-20, 26 and 27, characterized in that the polymers are living.



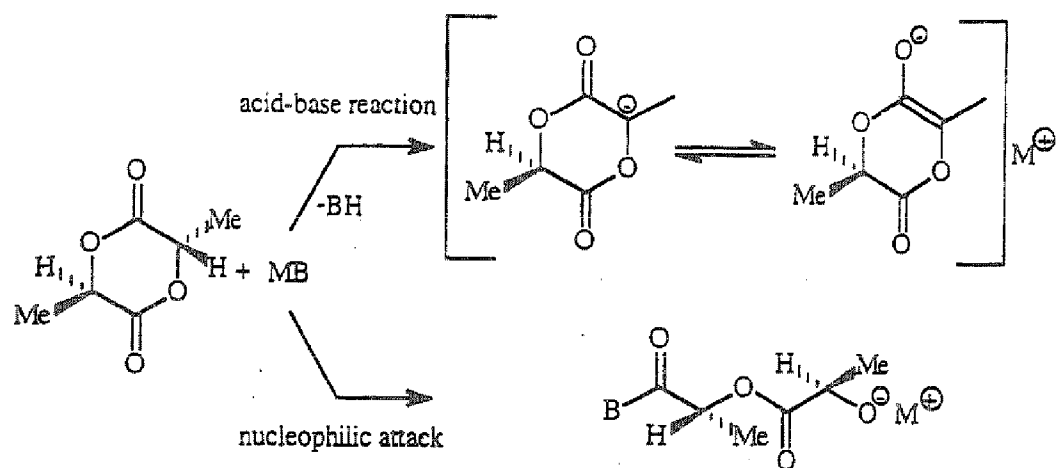


Fig. 1

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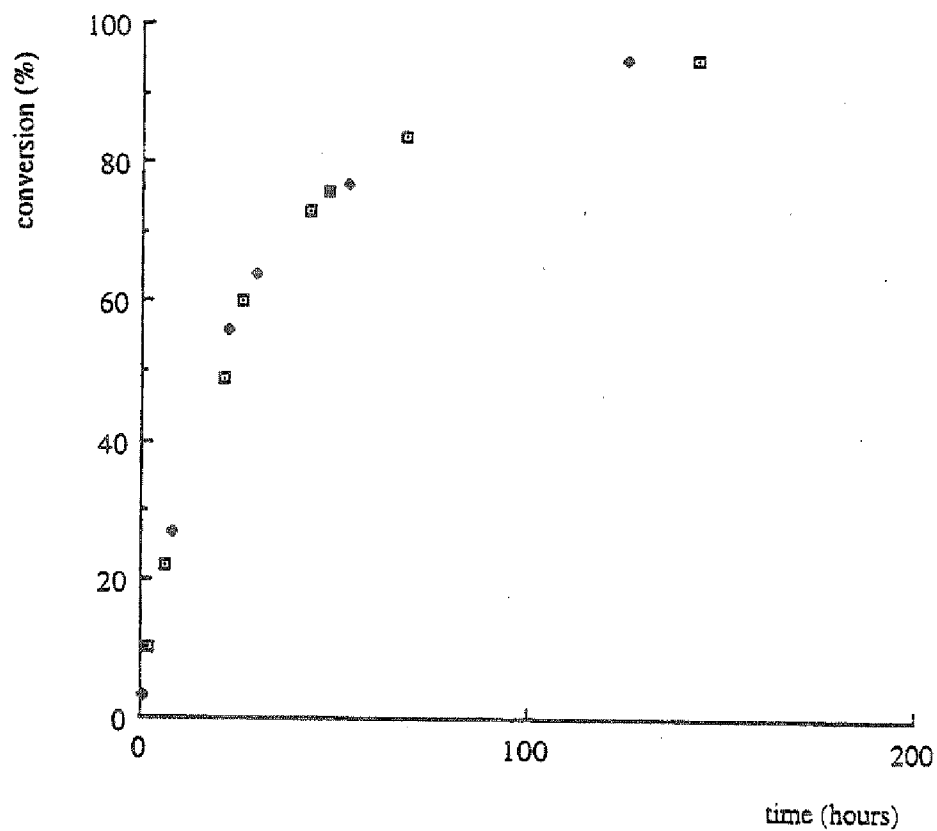


Fig. 2

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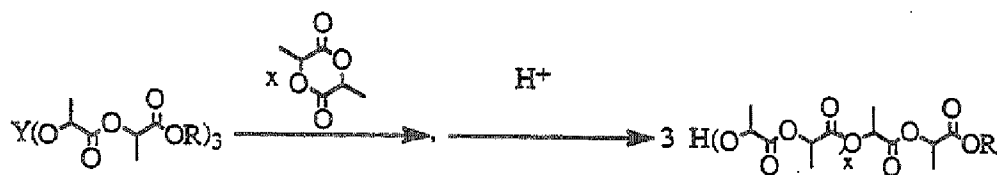
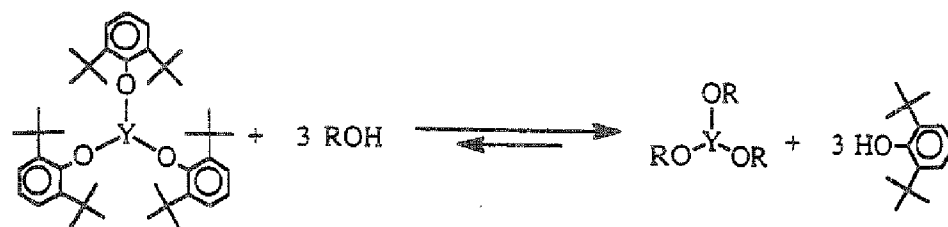


Fig. 3

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# INTERNATIONAL SEARCH REPORT

Int. Patent Application No.  
PCT/NL 95/00442

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 C08G63/82 C08G64/30 C08G65/10 C08G67/04 B01J31/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 C08G B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,93 18080 (E. I. DU PONT DE NEMOURS AND COMPANY) 16 September 1993  see claims 1-14	1-4, 7-11, 14-20, 24-29
X	WO,A,91 05001 (E. I. DU PONT DE NEMOURS AND COMPANY) 18 April 1991  see claims 1-29	1-4, 7-11, 14-20, 24-29

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

17 April 1996

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# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/NL 95/00442

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9318080	16-09-93	US-A- 5235031	10-08-93
WO-A-9105001	18-04-91	US-A- 5028667	02-07-91
		AT-T- 124709	15-07-95
		AU-B- 6624490	28-04-91
		CA-A- 2066029	30-03-91
		CN-A- 1051367	15-05-91
		DE-D- 69020739	10-08-95
		DE-T- 69020739	23-11-95
		EP-A- 0493529	08-07-92
		GR-A- 90100721	20-01-92
		JP-T- 5500982	25-02-93
		US-A- 5095098	10-03-92

Form PCT ISA 210 (patent family annex) (July 1992)

